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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/063,553	05/02/2002	Audrey Goddard	P3230R1C001-168	9988

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EXAMINER	
KOLKER, DANIEL E	
ART UNIT	PAPER NUMBER
1649	

SHORTENED STATUTORY PERIOD OF RESPONSE	NOTIFICATION DATE	DELIVERY MODE
3 MONTHS	12/22/2006	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Notice of this Office communication was sent electronically on the above-indicated "Notification Date" and has a shortened statutory period for reply of 3 MONTHS from 12/22/2006.

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TT

Office Action Summary	Application No.	Applicant(s)	
	10/063,553	GODDARD ET AL.	
	Examiner	Art Unit	
	Daniel Kolker	1649	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10 October 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *6,7,9 and 11-17* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *6,9 and 12-17* is/are rejected.

7)☒ Claim(s) *7 and 11* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *10/10/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. The remarks, amendments to the claims and the specification, and declaration filed 10 October 2006 have been entered. Claims 6 – 7, 9, 11 – 17 are pending and under examination.

2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Withdrawn Rejection and Objections

3. The following rejections and objections set forth in the previous office action are withdrawn:

A. The rejection under 35 USC §§ 101 and 112, first paragraph, for lack of specific and substantial utility is withdrawn in light of the arguments. In previous office actions, the examiner had argued that the results of experiments using nucleic acid were not sufficiently predictive of the expression patterns of the encoded proteins and therefore did not allow one of skill in the art to know the use of the proteins now claimed. In the remarks submitted 10 October 2006, applicant argues that the evidence of record support the assertion that protein expression levels are correlated with mRNA levels. Upon further consideration, the examiner agrees with applicant's reasoning, when the assay used to measure such mRNA levels is the RT-PCR assay that uses tissue-matched control samples, described on p. 140 of the specification. Therefore one of skill in the art would be able to use the proteins now claimed to distinguish normal stomach from stomach tumor or normal rectum from rectum tumor, as asserted by applicant.

The examiner notes that while the arguments refer to the declaration by Dr. Scott, which has been considered, the declaration is not on point to the instant invention. The declaration describes correlations between protein expression levels and nucleic acid data obtained from microarrays. Microarrays were not used in the experiments described on p. 140 of the specification.

Maintained Rejections and Objections

Priority

4. The effective filing date for all pending claims is 24 August 2000. Applicant did not traverse this statement and thus the examiner's determination stands for the reasons of record.

Claim Rejections - 35 USC § 112

5. Claims 6, 9, and 12 – 17 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the protein of SEQ ID NO:48, does not reasonably provide enablement for for polypeptides which either consist of, or alternatively comprise, residues 32 – 49 or 111-190 of SEQ ID NO:48, or for variants at least 95% identical to SEQ ID NO:48 which can make antibodies used to detect the full-length protein. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

This rejection is maintained for the reasons of record. Briefly, the claims are drawn to fragments of SEQ ID NO:48 and variants of the same protein. The specification discloses a single instance of a nucleic acid that encodes SEQ ID NO:48 which is differentially expressed in tumor vs. control tissue, wherein the control is form the same tissue as the tumor. The specification fails to disclose which residues are encoded by this nucleic acid, but does disclose that it is considerably less than the full length protein. See p. 140, which discloses that the fragment is approximately 200 – 600 bp in length. As three base-pairs encode a single amino acid, this corresponds to a nucleic acid which encodes 66-200 amino acids. The specification provides no evidence whatsoever that amino acids 32 – 49 or 111 – 190, recited in claims 6, 9, 14, and 15, are differentially expressed in any tumor compared to control. The specification does not disclose those structural elements of SEQ ID NO:48 which must be retained such that a variant at least 95% identical thereto will retain the proper differential expression pattern. The prior art teaches that one cannot predict the relationship between a particular nucleic acid sequence and whether or not the entire sequence, or encoded protein, is differentially expressed in cancer. The enclosed article by Coulson (2000. Cancer Research 60:1840-1844) is particularly relevant to this matter. Coulson teaches that a splice variant containing as few as 50 additional base pairs out of over a thousand in the mRNA can be used for cancer diagnosis, whereas the variant lacking this small additional piece is not differentially expressed in cancer versus normal control tissue. These splice variants differ by only 5% (50 base pairs out of 1000). Thus the art indicates that there is no particular relationship between nucleic acid sequence and use as a cancer diagnostic when the nucleic acid sequence is varied. Given the lack of guidance as to which regions of the protein variants of claims 14 – 15 must be preserved, it would take undue experimentation to determine both how to make and how to use these variants, since the only asserted use for the proteins is as a cancer diagnostic.

Additionally, the requirement that the protein variant be able to produce an antibody which can be used to detect the protein of SEQ ID NO:48 in stomach or rectum tissues does not indicate which structures can be varied or must be retained. The claims do not require that the protein variant itself is overexpressed in any tissue, and the art of record (Hopp et al. 1981) teaches that any six amino acids are sufficient to produce an antibody when administered to a mammal.

Claims 14 – 17 do not require that any particular structure be present, nor do the claims teach the artisan which regions are sufficient to make an antibody, or which ones are necessary to ensure that the antibody will "specifically detect the polypeptide of SEQ ID NO:48" as recited in claims 14 and 15. For an antibody to "specifically detect" a protein means that it will not detect other proteins, thus ensuring to the artisan who uses it that the target protein in question (here, SEQ ID NO:48) is what is actually identified by the antibody. The specification does not teach the artisan which regions of SEQ ID NO:48 are required so that the resultant antibody will have the required specificity.

Thus given the breadth of the claims, in that they encompass far more than what is actually disclosed, the lack of working examples, or even of prophetic examples, of how to use residues 32-49 or 111-190 of SEQ ID NO:48, the lack of guidance in the specification as to which regions of SEQ ID NO:48 or of those small fragments (i.e. residues 32-49 or 111-190) are either necessary or sufficient to make the antibodies with the specificity recited in claims 14 and 15, and the lack of guidance as to which regions of the proteins should be retained in the variants, it would take undue experimentation for the artisan to both make and use the invention commensurate in scope with the claims.

On p. 26 of the remarks, applicant cites MPEP § 2164.01(c), which states in part that "if any use is enabled... the application is enabling for the claimed invention." While this is of course true, applicant is directed to the more relevant section of MPEP, which particularly deals with the question of whether or not enablement is commensurate in scope with the claims. See for example MPEP § 2164.08, which states:

> All questions of enablement are evaluated against the claimed subject matter. The focus of the examination inquiry is whether everything within the scope of the claim is enabled.... The Federal Circuit has repeatedly held that "the specification must teach those skilled in the art how to make and use the full scope of the claimed invention without undue experimentation'." In re Wright, 999 F.2d 1557, 1561, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993). [emphasis added]

Here, the full scope of the claims includes variants which are not demonstrated to be differentially expressed in cancers, and the art teaches it is unpredictable whether or not the proteins would be differentially expressed in cancers. The claims thus include an unreasonable number of protein variants for which a use would have to be discovered by the skilled artisan. Given the lack of guidance in the specification, the burden would be on the artisan to discover how to use the proteins, and the artisan would have to thus resort to undue experimentation to determine this.

6. Claims 14 – 17 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a written description rejection.

This rejection is maintained for the reasons of record. Briefly, the claims are drawn to polypeptides at least 95% identical to SEQ ID NO:48, or to residues 32-49 or 111-190 of SEQ ID NO:48, wherein the resultant protein can make an antibody to specifically detect SEQ ID NO:48. The specification discloses only a single member of the broad genus, namely SEQ ID NO:48 itself. The examiner concedes that making variants is within the skill of the artisan, and testing antibodies is within the skill of the artisan. However, whether or not the artisan is so skilled does not indicate that the specification discloses that applicant was in possession of the claimed invention.

Applicant refers to example 14 of the written description guidelines for support for the argument that claims to variants at least 95% identical to a disclosed sequence with appropriate functional language are generally considered to meet the written description requirement. While this is true, in the instant case the functional language recited, i.e. an ability to generate an antibody, is so broad as to be irrelevant. The art of record (Hopp et al. 1981) indicates that any six consecutive amino acids are sufficient to induce an antibody response. As claims 14 and 15 require 95% and 99% amino acid identity to the reference sequence, adding the functional language "wherein said isolated polypeptide or a fragment thereof can be used to generate an antibody which can be used to specifically detect the polypeptide of SEQ ID NO:48 in stomach or rectum tissue samples" fails to further distinguish the claimed variants from those described by sequence identity alone. Applicant argues, pn pp. 27 – 28 of the remarks, that there is

sufficient guidance on how to make the variants and cites *In re Wands* in support of this argument. This argument is not on point, as the question is not one of enablement, but rather of written description.

Applicant also cites *In re Wallach*. This case was cited in the remarks filed 17 April 2006. The issues were addressed by the examiner in the previous office action (see particularly pp. 11 – 12 of the previous office action. In *Wallach*, the court found that the specification failed to provide a sufficient written description of the claimed chemical invention, because it did not disclose those features which distinguish the genus of claimed compounds. On p. 22 of the remarks, applicant argues that the facts in the instant case are very close to those in *Wallach*. To the extent that that is true, it would tend to support the examiner's rejection for lack of written description, as the court ruled in *Wallach* that the examiner and the Board of Patent Appeals and Interferences were both correct in their conclusions that the specification did not describe the claimed invention.

7. Claims 6, 9, 12 – 17 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new matter rejection.

Claims 6, 9, and 14 – 17 each encompass polypeptides comprising amino acid sequences selected from residues 32-49 and 111-190 of SEQ ID NO:48, or polypeptides at least 95% identical thereto, or chimeric proteins comprising same. The examiner is unable to find support for proteins comprising these regions in the specification as originally filed. In the remarks filed 10 October 2006, applicant argues that since certain fragments have been described in a broad, generic manner, the claimed invention was described in the original disclosure. Applicant's arguments have been fully considered but they are not persuasive. Neither of the fragments, now identified by residue number, were described in the disclosure as originally filed. Without reference to the actual fragments and proteins and variants comprising same, the originally-filed disclosure does not in fact provide support for the claims which recite them. Thus the rejection stands for the reasons of record.

Conclusion

8. Claims 6, 9, and 12 – 17 are rejected.

9. Claims 7 and 11 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

10. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Daniel Kolker whose telephone number is (571) 272-3181. The examiner can normally be reached on Mon - Fri 8:30AM - 5:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Janet Andres can be reached on (571) 272-0867. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

DK

Daniel E. Kolker, Ph.D.
December 13, 2006

ROBERT C. HAYES, PH.D.
PRIMARY EXAMINER